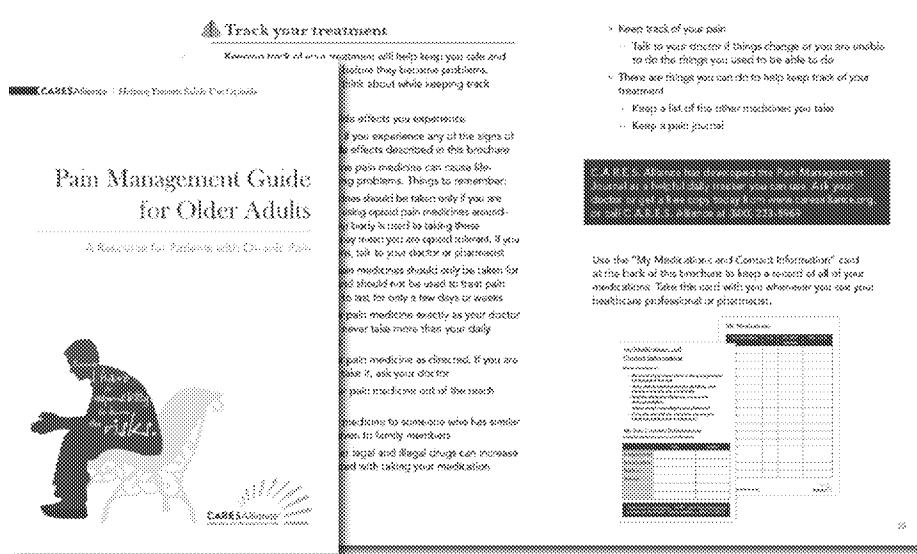


5.3.4 Pain Management Guide for Older Adults

The Pain Management Guide for Older Adults is a resource for older patients that describes how to talk openly about their chronic pain with their HCP. This resource also contains information for patients on how to safely use and handle their prescription opioid analgesics (**Figure 37**).

Figure 37: Pain Management Guide for Older Adults



5.3.5 Online Resources Center for Patients

The content for patients discussed above is available for download and/or print ordering at the www.caresalliance.org website. This site functions as a one-stop resource for patients interested in ensuring the safe use of their opioid medications (**Figure 38**).

Figure 38: The C.A.R.E.S. Alliance Website Patient Resources Page

Improving Patient Safety in Pain Management

[Home](#) | [Contact Us](#) | [Resources](#) | [Print Version](#)

People With Pain

Controlling Your Acute Response to Chronic Pain

Welcome to C.A.R.E.S. Alliance!

Right now, because of America's love affair with pain and especially for adults, for many, their health don't just mean finding an effective pain management. In addition, added value to improving quality of life.

C.A.R.E.S. Alliance is a web patient service initiative to aid pain management. Our goal is to help health care professionals and patients to work more closely together to better reduce low intensity and short-term pain. Interested in these services along with pain? Visit the links throughout.

Resources

To help people and pain doctors manage their pain and understand the importance of the interdisciplinary team, C.A.R.E.S. Alliance has developed several resources for you to use. Please click below to learn more about our offerings of free materials about to live successfully with pain.

Contact Us

To reduce the risks of pain medications, educational materials are produced and freely offered through the links below.

Event Calendar

Reference Library

Disclaimer

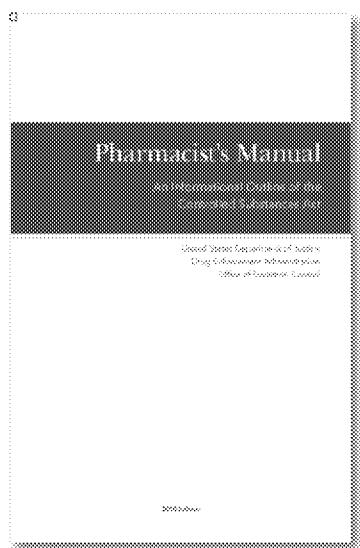
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5.4 Pharmacist Support Tools

5.4.1 Pharmacist's Manual: An Informational Outline of the Controlled Substances Act

The Pharmacist's Manual is prepared by the Drug Enforcement Agency, Office of Diversion Control, as a guide to assist pharmacists in their understanding of the Federal Controlled Substances Act and implementing its regulations as they pertain to the pharmacy profession (**Figure 39**).

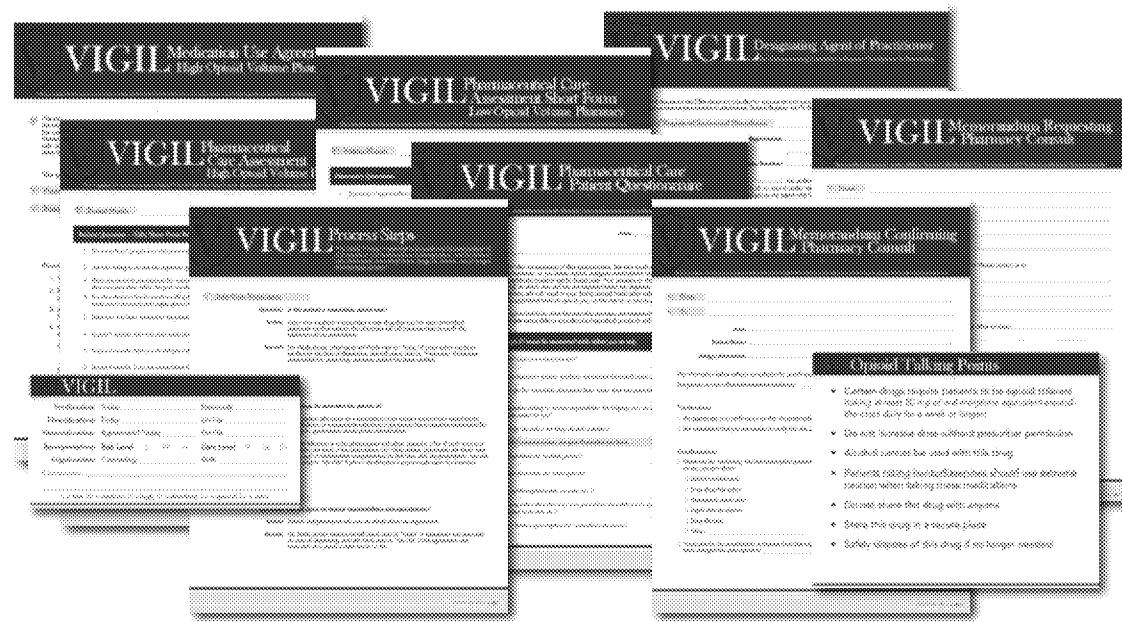
Figure 39: Pharmacist's Manual: An Informational Outline of the Controlled Substances Act



5.4.2 VIGIL Pharmacist Toolkit

The VIGIL Pharmacist Toolkit provides recommended steps that pharmacists should take when dispensing opioids to patients in order to mitigate the risk of abuse, misuse, and diversion. Steps include Verification, Identification, Generalization, Interpretation, and Legalization (VIGIL). A variety of tools are available to help the pharmacist ensure that prescription opioids are dispensed under conditions that optimize their safe use (**Figure 40**).

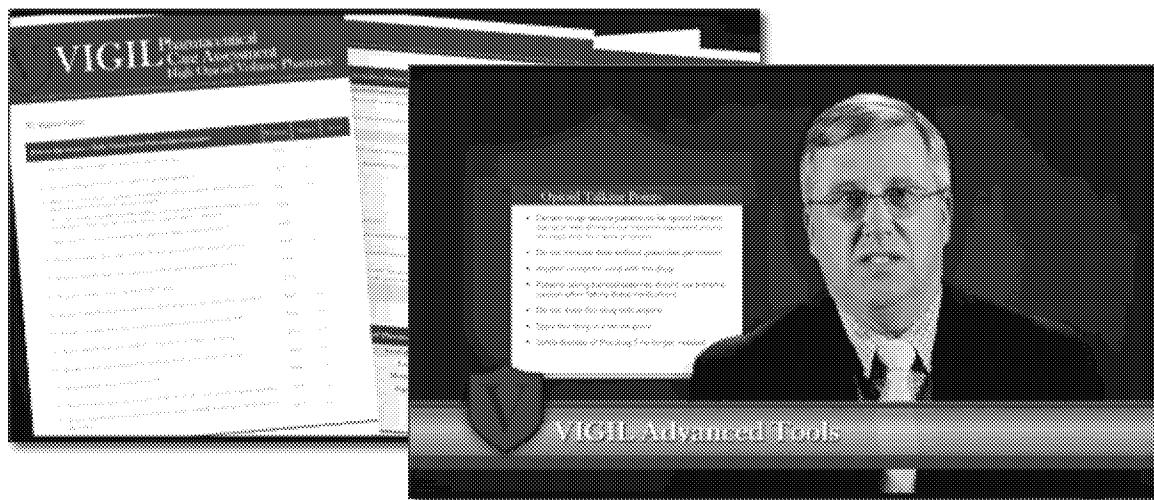
Figure 40: VIGIL Pharmacist Toolkit



5.4.3 VIGIL Education and Implementation Video

In this brief video, David Brushwood, RPh, JD, Professor of Pharmacy Health Care Administration at the University of Florida, discusses the conflicting therapeutic imperatives faced by pharmacists dispensing opioids to patients with chronic pain in a highly regulated environment. He discusses ethics of pain management, potential “red flags” for misuse, abuse, or diversion of pain medications, and adherence to Drug Enforcement Administration regulations on dispensing of controlled substances. He introduces his key to compliance with responsible opioid dispensing practices—Verification, Identification, Generalization, Interpretation, and Legalization (VIGIL)—and provides background on the VIGIL process and the available VIGIL tools (**Figure 41**).

Figure 41: VIGIL Education and Implementation Video



6. REMS ASSESSMENT PLAN

6.1 Overview

Mallinckrodt will conduct periodic assessments of the extent to which the REMS components are meeting the goals or whether the goals or particular elements should be modified. The assessment plan includes assessment of the performance of the REMS education plan (including HCP knowledge and behavior related to safe use conditions) as well as surveillance and monitoring of patient outcomes, including REMS-related adverse events of interest. The following sections summarize the sources of information that will be used in conducting the assessments.

6.2 Patient Knowledge, Attitude, and Behavior Surveys

Knowledge, Attitude, and Behavior (KAB) surveys will be conducted with patients in order to assess their comprehension of the EXALGO risks and key safe use information. The survey period will begin approximately nine months after the approval of the updated Full Prescribing Information and EXALGO.

The methodology and protocol for the KAB surveys and the survey instrument will be modified after the product labeling and Medication Guide are finalized and will be provided to the FDA at least 90 days before the surveys are administered. The protocols will include the sample size and confidence intervals associated with that sample size, how the sample will be selected, specific selection criteria, how the participants will be recruited, how and when the surveys will be administered, and an explanation of the design features included to minimize bias.

6.3 Distribution and Dispensing of the Medication Guide

Mallinckrodt will periodically assess the distribution and dispensing of the Medication Guide for EXALGO in accordance with 21 CFR §208.24 as detailed in the description of the Medication Guide above (section 2.3). The KAB surveys described above will also assess this by querying patients about whether they received a Medication Guide when they obtained their prescriptions for EXALGO. As a part of standard pharmacovigilance, when an adverse event is reported, a Mallinckrodt representative will ask the reporter whether an EXALGO Medication Guide was issued to the patient in question. This information will be provided in the regular assessment reports for the REMS.

6.4 Report on Status of Prescriber Education

The required REMS assessment that will be submitted by Mallinckrodt will include a narrative summary of the education program, which will incorporate a report of the status of the education program for HCPs. This report will consist of the topics included in the education program, educational venues, number of EXALGO REMS educational events hosted by Mallinckrodt, total number of participants, and website utilization statistics. This report will also include the results

of an outcome and evaluation survey that will be given to participants as well as the number of completed ECFs. In addition, Mallinckrodt will detail all requests for training (e.g., geography, HCP demographics).

An assessment of training and utilization statistics for prescribers will include the following:

- ∞ The number of prescribers newly trained in the EXALGO REMS program (during the reporting period and cumulative)
- ∞ The number of prescribers who wrote one or more prescriptions for EXALGO (during the reporting period and cumulative)
- ∞ The proportion of prescribers who wrote one or more prescriptions for EXALGO and who were trained (during the reporting period and cumulative)
- ∞ The proportion of prescribers who wrote one or more prescriptions for EXALGO and who were not trained (during the reporting period and cumulative)
- ∞ The number of prescribers who were re-trained after two years (within the reporting period and cumulative)

6.5 Prescriber Knowledge, Attitude, and Behavior Surveys

KAB surveys will be conducted with prescribers in order to assess their comprehension of the serious risks of EXALGO as outlined in the REMS objectives. The prescriber surveys will also measure understanding of appropriate prescribing and safe use of EXALGO. The survey period will begin approximately nine months after the approval of the updated Full Prescribing Information and EXALGO REMS.

The methodology and protocol for the KAB surveys and the survey instrument will be contained in the KAB Survey protocol. The protocols will include the sample size and confidence intervals associated with that sample size, how the sample will be selected, specific selection criteria, how the participants will be recruited, how and when the surveys will be administered, and an explanation of the design features included to minimize bias.

6.6 Measures to Increase Awareness and Knowledge of EXALGO REMS Material

If Mallinckrodt becomes aware of inadequate understanding of the serious risks and appropriate use associated with EXALGO, it will employ interventions up to and including individual phone calls and additional training. Mallinckrodt will employ conventional methods (Dear Healthcare Professional Introductory Letters, etc.) as well as non-standard communications, such as telephone calls and personal visits from Medical Science Liaisons, to reach out to HCPs to improve awareness and understanding of the serious risks and appropriate prescribing associated with EXALGO. Should one or more of the REMS component tools be shown to be ineffective, Mallinckrodt will submit a revised supplement to the FDA for the specified REMS tool prior to implementing any changes to the approved REMS.

Mallinckrodt will continue to implement a voluntary Education Escalation Program, which uses a structured system to contact identified EXALGO prescribers who have not submitted a completed ECF. Mallinckrodt will continue to evaluate and improve this program to ensure that as many HCPs as possible are educated.

6.7 Adverse Event Monitoring, Analysis, and Reporting

6.7.1 Mallinckrodt Pharmacovigilance Adverse Event Monitoring

The activities occurring under this REMS will be integrated with Mallinckrodt's pharmacovigilance program to ensure proper surveillance, monitoring, and reporting of adverse events (**Table 7**). Mallinckrodt's safety staff will collect as much information as possible about these adverse events. The pharmacovigilance program will be implemented through standard operating procedures to ensure a systematic process for capturing, evaluating, investigating, responding to, and reporting adverse events. Spontaneous adverse event reports meeting the criteria for expedited reporting to the agency, as defined in 21 CFR § 314.80, as well as other reports designated as REMS-related adverse events of interest (see below), will be submitted to the FDA within 15 calendar days. Adverse event reports will be individually reviewed and collectively evaluated to determine if changes to the REMS education could help to further mitigate the risks.

6.7.2 FDA Adverse Event Reporting System (AERS)

The FDA AERS database provides comprehensive data on reports of adverse events associated with physician visits as well as consumer and pharmaceutical industry reports, but also allows for comparison of proportional reporting rates and empirical Bayes geometric means of adverse events among drugs (**Table 7**). The FDA AERS data will be integrated with Mallinckrodt's database to assess patient outcomes and overall REMS performance.

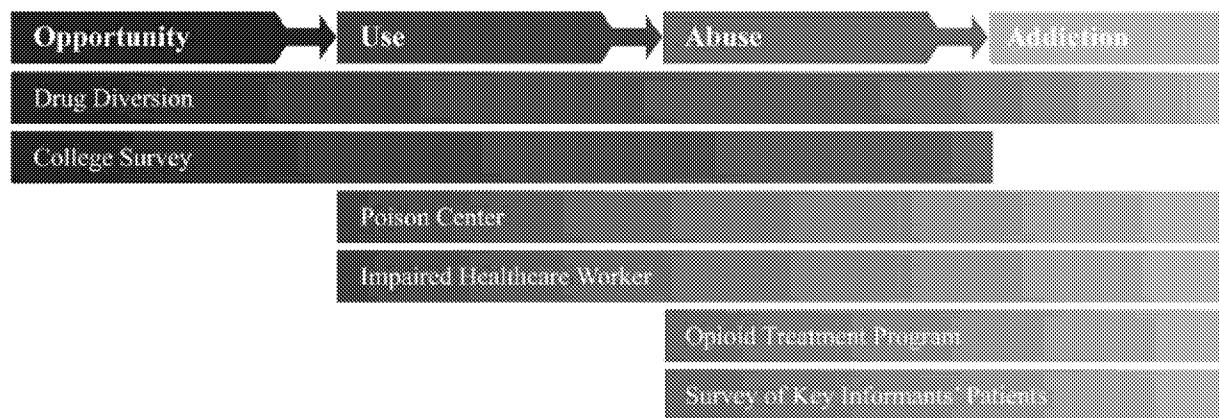
Table 7: Post-approval Adverse Event (AE) Reporting

Description	Outcomes
Mallinckrodt Pharmacovigilance	
∞ Spontaneous adverse event reports meeting the criteria for expedited reporting to the agency, as defined in 21 CFR§314.80, will be submitted within 15 calendar days	∞ Death—All spontaneous and possibly related reports of death
∞ All other reportable adverse events will be submitted to the agency in the Periodic Safety Update Reports	
∞ Death—All spontaneous and possibly related reports of death	
∞ Overdose—All overdose	
∞ Misuse, abuse, addiction, and diversion	
∞ All serious adverse events associated with suspected misuse	
∞ All adverse events associated with manipulation of the tablet	
∞ All adverse events associated with suspected abuse, addiction, and diversion	
∞ Inappropriate prescribing/medication errors	
∞ All non-accidental pediatric exposures associated with an adverse event (serious and non-serious)	
∞ All actual and potential medication error reports regardless of patient outcome	
∞ All adverse events associated with use in opioid non-tolerant patients	
∞ All adverse events associated with use in patients with acute or post-operative pain or “as needed” (prn) use	
∞ Accidental exposures—All accidental exposures including asymptomatic reports (children and adults)	
FDA AERS	
Database that not only provides comprehensive data on reports of AEs associated with physician visits as well as consumer and pharmaceutical industry reports, but also allows for comparison of proportional reporting rates and empirical Bayes geometric means of AEs among drugs	∞ Death ∞ Overdose (fatal and non-fatal) ∞ Misuse, abuse, and addiction ∞ Inappropriate prescribing ∞ Medication errors ∞ Accidental exposures/ingestion

6.7.3 Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System (Ongoing)

The RADARS System collects timely, product-specific and geographically specific data on prescription drug abuse, misuse, and diversion. RADARS contains individual programs that assess different aspects of prescription drug use and abuse (Drug Diversion, College Survey, Poison Center, Impaired Health Care Worker, Key Informant, Opioid Treatment Program, and Survey of Key Informant’s Patients) (**Figure 42**).

Figure 42: Components of RADARS Surveillance



Source: Adapted from RADARS Systems. RADARS programs. <http://www.radars.org/Home2/Programs.aspx>. Accessed September 21, 2011.

6.7.3.1 Drug Diversion Program

This program provides quarterly reports of the number of new cases of diversion, defined as the number of new instances of pharmaceutical diversion reported to or investigated by one of 300 diversion units or regulatory boards during the previous quarter. Cases are assigned to the three-digit ZIP code where the case occurred.

6.7.3.2 College Survey

This program is an online questionnaire collecting data from self-identified students attending a two- or four-year college, university or technical school at least part-time during the specified sampling period. Data are collected at the completion of the fall and spring academic semesters/quarters and at the end of the summer. Cases are assigned to the reported three-digit ZIP code of the college student's residence.

6.7.3.3 Poison Center Program

Participating poison centers (50-57) report cases for drugs of interest on a weekly basis. Cases are defined as any intentional exposure managed by participating poison centers for the drugs of interest (e.g., EXALGO). Intentional exposures are used as surrogates for misuse and abuse. These intentional exposure reasons include suicide, intentional misuse, abuse, intentional unknown, and withdrawal cases. Cases are assigned to the reported three-digit ZIP code of the exposed individual's residence. In addition, individual EXALGO-specific cases will be communicated monthly to and processed by the Mallinckrodt Pharmacovigilance personnel.

6.7.3.4 Impaired Healthcare Worker

This program is a subset of the Drug Diversion, Poison Center, Opioid Treatment Program and Survey of Key Informants' Patients program where the cases reported are from a healthcare worker.

6.7.3.5 Opioid Treatment Program

This program is composed of 75 participating methadone treatment programs. Patients enrolling at these treatment centers are asked to complete an anonymous questionnaire, which includes questions concerning the patient's drugs of choice, drug use in the past month, lifetime drug abuse, age at first use, and the primary source of the abused drugs. Cases are defined as self-reported use of a prescription or illicit opioid to get high in the past 30 days. Cases are assigned to the reported three-digit ZIP code of the patient's residence.

6.7.3.6 Survey of Key Informants' Patients

This program is composed of patients in treatment facilities recruited by Key Informants to complete an anonymous questionnaire that includes questions concerning the patient's drugs of choice, drug use in the past month, lifetime drug abuse, age at first use, and the primary source of the abused drugs. Cases are defined as self-reported use of a prescription or illicit opioid to get high in the past 30 days. Cases are assigned to the reported three-digit ZIP code of the patient's residence.

6.8 Internet and Media Monitoring

Mallinckrodt will provide a report of Internet discussions and media coverage of EXALGO. This will include awareness and attractiveness of EXALGO to the opioid-abusing population. This report will also include discussions or reports of misuse, abuse, and attempts or instructions for defeating the extended-release system.

6.9 EXALGO Utilization

Mallinckrodt will utilize the available prescription transaction and longitudinal data (e.g., IMS) to analyze EXALGO utilization patterns. Mallinckrodt conducts outreach and interventions as necessary to address concerns regarding irregular or unusual patterns in the prescribing of EXALGO.

6.10 New Assessment and Monitoring Methods

Appropriate prescribing is a key element of safe use of EXALGO, and particularly use of the 32 mg tablet. Reducing the risk of unintentional overdose requires proper patient selection (e.g., use only in opioid-tolerant patients) and proper dosing and administration (e.g., appropriate conversion and titration) as outlined in the Full Prescribing Information and EXALGO REMS education information. Mallinckrodt will employ enhanced monitoring and assessment activities to confirm appropriate prescribing of the 32 mg tablet. In addition, Mallinckrodt is willing to work with the FDA on designing an observational study that will be used to verify appropriate prescribing and patient outcomes.

6.10.1 Chart Review Studies

Mallinckrodt conducted a pilot study to assess the feasibility, design, and sample size for a planned study to determine the extent to which prescribers are following the EXALGO Full Prescribing Information. Chart review studies will be used to evaluate appropriate prescribing of EXALGO. Direct evaluation of patient charts provide the ability to verify appropriate prescribing practices from actual data, including: patient selection (e.g., use in opioid-tolerant patients, use in adults only); dosing and administration (e.g., appropriate conversion and titration, reduction of starting dose after conversion, use with other sedating medications [e.g., benzodiazepines, other ER/LA opioid analgesics]).

6.10.2 Additional Postapproval Evaluation and Study (proposed)

Mallinckrodt is willing to work with the FDA on designing an observational study evaluating the incidence of abuse, misuse, addiction, and overdose in patients taking 32 mg/day EXALGO. If such an observational study is required for the approval of the 32 mg strength, Mallinckrodt will ensure the study design is compliant with all current regulations and guidance.

6.10.3 System and Program Performance

A narrative summary will be submitted by Mallinckrodt with analysis and evaluation of the EXALGO risk mitigation strategy.

Pursuant to 21 CFR§ 314.80, Mallinckrodt will submit a quarterly periodic progress report for EXALGO to the FDA (EXALGO REMS assessment). The Global Drug Safety and Pharmacovigilance Department will write a narrative summary and analysis of the following adverse events reported during the reporting period (and cumulative):

- ∞ Death—All reports of death
- ∞ Overdose—All reports of overdose
- ∞ Misuse, abuse, and addiction
 - All serious adverse events associated with suspected misuse
 - All adverse events associated with manipulation of the tablet
 - All adverse events associated with suspected abuse and addiction
- ∞ Inappropriate prescribing/medication errors
 - All non-accidental pediatric exposures associated with an adverse event (serious and non-serious)
 - All actual and potential medication error reports regardless of patient outcome
 - All adverse events associated with use in opioid non-tolerant patients

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- All adverse events associated with use in patients with acute or post-operative pain or “as needed” (prn) use
- All adverse events associated with healthcare professional-directed manipulation of the tablet
- ∞ Accidental exposures—All accidental exposures, including asymptomatic reports (children and adults)
- ∞ RADARS Surveillance System reports of overdose (fatal and non-fatal), misuse, abuse, addiction, accidental ingestion (particularly in children), pediatric exposure, inappropriate prescribing, and diversion
- ∞ Internet and media monitoring—Abuse of EXALGO and route of administration, if known
- ∞ FDA-AERS—Death, overdose (fatal and non-fatal), misuse, abuse, addiction, inappropriate prescribing, medication errors, accidental exposures/ingestion
- ∞ Narrative summary and analysis of the surveillance activities during the reporting period (and cumulative)
- ∞ A summary of all changes to the EXALGO REMS that were implemented during the reporting period
- ∞ A report of periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
- ∞ A summary report of all educating initiatives
- ∞ An assessment of healthcare professional and patient understanding of the risk, appropriate prescribing, and safe use of EXALGO (the results of surveys administered to prescribers and patients)
- ∞ All information will be analyzed and summarized in aggregate and separately for the 32 mg tablet whenever possible
- ∞ Based on the information provided, an assessment and conclusion of whether the EXALGO REMS is meeting its goals, and whether modifications to the program are needed
- ∞ Report of additional assessment and monitoring (e.g., chart study, postapproval study)

6.10.3.1 Proposed Intervention to Potential Non-Compliance or Potential Signals

Mallinckrodt will review all cases of special interest and will employ conventional methods (Dear Healthcare Professional Introductory Letters, etc.), as well as non-standard communications such as telephone calls and personal visits from Medical Science Liaisons, to reach out to HCPs in response to a signal. The REMS Element to Assure Safe Use (ETASU) will be evaluated in the context of the performance of the entire REMS program to determine the extent to which the REMS ETASU is meeting the goal and objectives of the REMS, and whether or not the goals, objectives or the ETASU should be modified. If the REMS is shown to meet the goals of informing specified stakeholders of the risks associated with the responsible prescribing and use of EXALGO, Mallinckrodt will continue the REMS ETASU component tool. Should one or more of the REMS component tools be shown to be ineffective, Mallinckrodt will submit a revised supplement to the FDA for the specified REMS tool prior to implementing any changes to the approved REMS.

The additional non-REMS risk mitigation tools and activities will be continually evaluated for performance improvement in order to ensure that the program is maximizing patient outcomes.

6.11 Assessment of REMS Effectiveness

6.11.1 REMS Compliance Assessment Committee

An EXALGO REMS Compliance Assessment Committee (CAC) will comprise representatives from multiple functional areas within Mallinckrodt's organization, including Legal, Regulatory Affairs, Drug Safety and Pharmacovigilance, Medical Affairs, Clinical Development, and Marketing. The mission of the CAC is to coordinate and review the REMS for EXALGO. Mallinckrodt's CAC will review all cases of special interest (eg reports of overdose, addiction, abuse, misuse, and accidental ingestion), surveillance data, and other evaluations. The CAC will meet in person, electronically, or otherwise as often as necessary to fulfill its mission, but no less frequently than quarterly.

The responsibilities of this group are to:

- ∞ Review the EXALGO REMS program (including program material and the plans for the EXALGO REMS CAC and REMS Safety Advisory Board [RSAB])
- ∞ Regularly assess the ability of the REMS assessment plan to adequately evaluate the EXALGO REMS program
- ∞ Evaluate the progress of the EXALGO REMS program, including periodic assessments of data quality and timeliness, patient risk-benefit profile(s), and system performance
- ∞ Consider other factors outside of the EXALGO REMS that may impact the EXALGO REMS or patient safety, such as scientific, therapeutic, and regulatory developments
- ∞ Review the EXALGO REMS program performance and resolve issues (e.g., intervene in cases of inappropriate prescribing)

- ∞ Protect the safety of patients taking EXALGO
- ∞ Coordinate communications and interactions with the RSAB concerning EXALGO risks, EXALGO REMS progress and performance, and improvements to the EXALGO REMS and patient outcomes
- ∞ Obtain recommendations from the RSAB concerning EXALGO risks, EXALGO REMS progress and performance, and improvements to the EXALGO REMS and patient outcomes

6.11.2 REMS Safety Advisory Board

The EXALGO RSAB is an external clinical advisory board comprising clinical experts in the fields of pain and addiction medicine and epidemiologists who will interface with the EXALGO REMS CAC to review safety events. The charter of this group is to act in an advisory capacity to the EXALGO REMS CAC to ensure the risk-benefit balance in patients taking EXALGO. The RSAB will also monitor the EXALGO REMS program to ensure that it is adequately addressing the stated goals and objectives (**Figure 43** depicts the relationship between the CAC and the RSAB).

The responsibilities of the RSAB are to:

- ∞ Review the EXALGO REMS program (including program material)
- ∞ Review the plans for the EXALGO REMS CAC and RSAB
- ∞ Advise the EXALGO REMS CAC on the ability of the REMS to meet its stated goals and objectives
- ∞ Advise the EXALGO REMS CAC on the ability of the REMS assessment plan to adequately evaluate the EXALGO REMS program
- ∞ Evaluate the progress of the EXALGO REMS program, including patient risk-benefit profile(s), periodic assessments of data quality and timeliness, and system performance
- ∞ Consider other factors outside of the EXALGO REMS that may impact the EXALGO REMS or patient safety, such as scientific, therapeutic, and regulatory developments
- ∞ Review the EXALGO REMS program and performance and assist the EXALGO REMS CAC in resolving potential issues
- ∞ Assist the EXALGO REMS CAC in protecting the safety of patients taking EXALGO
- ∞ Report on post-marketing patient safety and progress of the EXALGO REMS
- ∞ Make recommendations to the EXALGO REMS CAC concerning REMS risks, REMS training and communication materials, EXALGO REMS program and performance (i.e., execution of education), and improvements to the EXALGO REMS and patient outcomes

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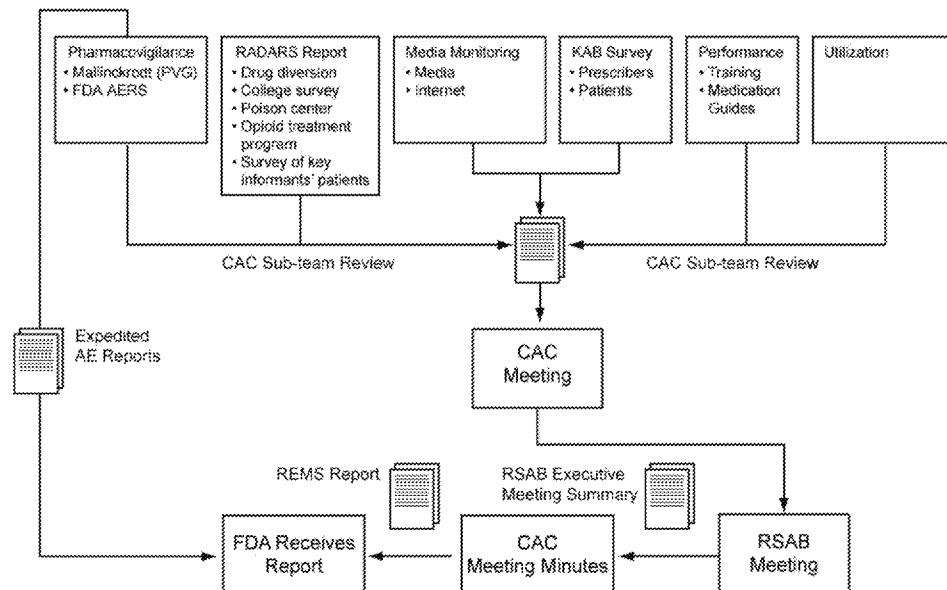
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The RSAB will also act in an advisory capacity to Mallinckrodt and the FDA to monitor the potential postapproval study for participant safety, appropriate prescribing, safe use, and data quality, and to evaluate the progress of the study.

Therefore, the responsibilities of the RSAB related to the potential postapproval study are:

- ∞ Evaluate the progress of the study, including periodic assessments of data quality and timeliness, recruitment, accrual and retention, participant risk versus benefit, and other factors that can affect study outcome
- ∞ Review study performance, make recommendations, and assist in the resolution of problems
- ∞ Protect the safety of the study participants
- ∞ Review ongoing prescribing practices and REMS-related events of interest and periodic analyses
- ∞ Report to FDA on the safety and progress of the study
- ∞ Make recommendations to Mallinckrodt and the FDA concerning continuation, termination, or other modifications of the study and/or the EXALGO REMS based on the observed beneficial or adverse effects of the study
 - The RSAB report will include recommendations to continue the study and EXALGO REMS/Risk Mitigation Strategy, continue the study and modify the EXALGO REMS/Risk Mitigation Strategy, or terminate the study.

Figure 43: Compliance Assessment Committee and REMS Safety Advisory Board



PVG = pharmacovigilance; FDA AERS = US Food and Drug Administration Adverse Event Reporting System; RADARS = Researched Abuse, Diversion and Addiction-Related Surveillance; KAB = Knowledge, Attitude, and Behaviors; CAC = Compliance Assessment Committee; RSAB = REMS Safety Advisory Board.

6.12 Timetable for Submission of Assessments

Mallinckrodt will submit REMS Assessments to the FDA six months, 12 months, and then annually from the date of approval of the REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment will conclude no earlier than 60 days before the submission date for that assessment time interval. Mallinckrodt will submit each assessment so that it will be received by the FDA on or before the due date.

REFERENCES

Butler SF, Budman SH, Fernandez KC, et al. Development and validation of the Current Opioid Misuse Measure. *Pain*. 2007;130:144-156.

Butler SF, Fernandez K, Benoit C, Budman SH, Jamison RN. Validation of the Revised Screener and Opioid Assessment for Patients with Pain (SOAPP-R). *J Pain*. 2008;9:360-372.

Carr DR, Jacox AK, Chapman CR, et al. *Acute Pain Management: Operative or Medical Procedures and Trauma, Clinical Practice Guideline No. 1*. Rockville, MD: Agency for Healthcare Research and Quality, US Department of Health and Human Services; 1992. AHCPR Pub. No. 92-0032; 116-117.

Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain*. 2009;10:113-130.

Fishman SM. *Responsible Opioid Prescribing: A Physician's Guide*. Washington, DC: Waterford Life Sciences; 2007.

Gourlay DL, Heit HA, Almahrezi A. Universal precautions in pain medicine: a rational approach to the treatment of chronic pain. *Pain Med*. 2005;6:107-112.

Gourlay DL, Heit HA. Universal precautions revisited: managing the inherited pain patient. *Pain Med*. 2009;10(S2):114-123

Moeller KE, Lee KC, Kissack JC. Urine drug screening: practical guide for clinicians. *Mayo Clin Proc*. 2008;83:66-76.

Passik SD, Kirsh KL, Whitcomb L, et al. A new tool to assess and document pain outcomes in chronic pain patients receiving opioid therapy. *Clin Ther*. 2004;26:552-561.

Tan G, Jensen MP, Thornby JI, Shanti BF. Validation of the Brief Pain Inventory for chronic nonmalignant pain. *J Pain*. 2004;5:133-137.

Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. *Pain Med*. 2005;6:432-442.

Wong D, Baker C. Pain in children: comparison of assessment scales. *Pediatr Nurs*. 1988;14:9-17.

Appendix A: EXALGO Labeling and EXALGO REMS Components

Tactic	Type	Stakeholder	Content	Brief Description	Image
Labeling					
Full Prescribing Information	Education	Prescriber, Pharmacist	A, B, C, D, E, F, G, H	The EXALGO Full Prescribing Information communicates the EXALGO risks, including the risk of abuse, misuse, overdose, and addiction, as well as information about the how to mitigate these risks. The prescribing information is attached to each bottle, provided with all educational material for HCPs, and accessible at www.exalgorems.com .	
Bottle Label	Education	Prescriber, Pharmacist, Patient	A, B, D	The bottle label will include a statement instructing the authorized dispenser that EXALGO is for opioid tolerant patients only and to provide a copy of the Medication Guide with each EXALGO prescription. The bottle label also contains the important reminder information for pharmacists, that EXALGO tablets should be swallowed whole and tablets should not be broken, crushed or chewed.	
Medication Guide	Education	Prescriber, Pharmacist, Patient	A, B, C, D, E, H	The EXALGO Medication Guide will be dispensed with each EXALGO prescription and will provide patients and caregivers with the most important information they should know about EXALGO, including risks, safe use, storage and disposal. Sufficient numbers of Medication Guides will be distributed to all pharmacies that dispense EXALGO.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

Tactic	Type	Stakeholder	Content	Brief Description	Image
Healthcare Professional Education Program Kit					
Healthcare Professional Education Program Kit	Education	Prescriber	A, B, C, D, E, F, G, H	The EXALGO REMS Healthcare Professional Education Program Kit contains all of the information necessary to complete the EXALGO REMS Education Program, including Full Prescribing Information, Medication Guide, Education Confirmation Form, Prescribing Brochure, and Safe Use and Handling Guide. It is disseminated with all Dear Healthcare Professional Introductory Letters and is available at all congress exhibits, for distribution by the EXALGO field force, and for download from www.exalgorems.com .	
Full Prescribing Information/Medication Guide	Education	Prescriber, Pharmacist, Patient	A, B, C, D, E	The EXALGO Full Prescribing Information communicates the EXALGO risks, including the risk of abuse, misuse, overdose, and addiction, as well as information about the how to mitigate these risks. The prescribing information is attached to each bottle, provided with all educational material for HCPs, and accessible at www.exalgorems.com . The EXALGO Medication Guide will be dispensed with each EXALGO prescription and will provide patients and caregivers with the most important information they should know about EXALGO, including risks, safe use, storage and disposal. Sufficient numbers of Medication Guides will be distributed to all pharmacies that dispense EXALGO.	
Dear Healthcare Professional Introductory Letter	Education	Prescriber	A, B, C, D, F, G, H	The Dear Healthcare Professional Introductory Letter will convey and reinforce the risks of abuse, misuse, overdose, and addiction with EXALGO therapy as well as the need to complete the EXALGO REMS Education Program. The introductory letter, along with contents of the education program, will be mailed within 60 days of approval of the 32 mg tablet strength to all EXALGO prescribers and prescribers most experienced in treating chronic pain with extended-release opioid agonists.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

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Tactic	Type	Stakeholder	Content	Brief Description	Image
Prescribing Brochure	Education	Prescriber	A, B, C, D, E, F, G, H	The Prescribing Brochure highlights essential information for HCPs who intend to prescribe EXALGO. It is disseminated with all Dear Healthcare Professional Introductory Letters, contained in the Healthcare Professional Education Program Kit, available for distribution by the EXALGO field force, and available for download from www.exalgorems.com .	
Education Confirmation Form (ECF)	Assessment	Prescriber	A, B, C, D, G, H	The Education Confirmation Form (currently the EXALGO Essential Information Form) is intended to confirm education/training in the EXALGO REMS Education Program and is designed to reinforce the most essential information, including risks and appropriate prescribing for HCPs who intend to prescribe EXALGO. This form will be modified to include the 32 mg tablet strength and associated risks.	
Safe Use and Handling Guide	Education, Enabler	Patient	A, B, C, D, E, G	The Safe Use and Handling Guide is an educational resource to enable prescribers to educate patients on the serious risks and in the safe use, storage, and disposal of EXALGO.	
Online Resources					
www.exalgorems.com	Education	Prescriber, Patient	A, B, C, D, E, F, G, H	The exalgorems.com website contains information about the EXALGO REMS program and serves as one method by which prescribers can complete the EXALGO REMS Education Program. The website serves as a central resource for obtaining all EXALGO REMS educational materials.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

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Tactic	Type	Stakeholder	Content	Brief Description	Image
www.exalgo.com	Education	Prescriber, Patient	A, B, C, D, G, H	The exalgo.com landing page offers direct access to the exalgorems.com website, along with an introduction consisting of the important safety information, prior to access of the exalgo.com website. The exalgo.com website contains important educational resources for both patients and HCPs, including risk information; proper dosing, administration, and handling of EXALGO; and patient counseling tools for prescribers. The site also contains a dedicated EXALGO REMS section where prescribers can access the EXALGO REMS Education Program online.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

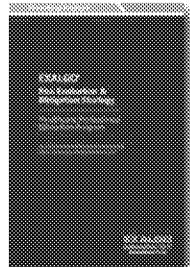
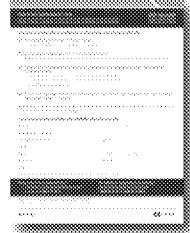
Appendix B: EXALGO REMS Education and Outreach Activities

Tactic	Type	Stakeholder	Content	Brief Description	Image
Print and Video					
Full Prescribing Information/Medication Guide	Education	Prescriber, Pharmacist, Patient	A, B, C, D, E, F, G, H	<p>The EXALGO Full Prescribing Information communicates the EXALGO risks, including the risk of abuse, misuse, overdose, and addiction, as well as information about the how to mitigate these risks. The prescribing information is attached to each bottle, provided with all educational material for HCPs, and accessible through the exalgorems.com website.</p> <p>The EXALGO Medication Guide will be dispensed with each EXALGO prescription and will provide patients and caregivers with the most important information they should know about EXALGO, including risks, safe use, storage and disposal.</p>	
Bottle Label	Education	Prescriber, Pharmacist, Patient	A, B, D	The bottle label will include a statement instructing the authorized dispenser that EXALGO is for opioid tolerant patients only and to provide a copy of the Medication Guide with each EXALGO prescription. The bottle label also contains the important reminder information for pharmacists, that EXALGO tablets should be swallowed whole and tablets should not be broken, crushed or chewed.	
Healthcare Professional Education Program Kit	Education	Prescriber	A, B, C, D, E, F, G, H	The EXALGO REMS Healthcare Professional Education Program Kit contains all of the information necessary to complete the EXALGO REMS Education Program, including Full Prescribing Information, Medication Guide, Education Confirmation Form, Prescribing Brochure, and EXALGO Safe Use and Handling Guide. It is disseminated with all Dear Healthcare Professional Introductory Letters and is available at all congress exhibits, for distribution by the EXALGO field force, and for download from www.exalgorems.com.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

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Tactic	Type	Stakeholder	Content	Brief Description	Image
Dear Healthcare Professional Introductory Letter	Education	Prescriber	A, B, C, D, F, G, H	The Dear Healthcare Professional Introductory Letter will convey and reinforce the risks of abuse, misuse, overdose, and addiction with EXALGO therapy as well as the need to complete the EXALGO REMS Education Program. The introductory letter, along with contents of the education program, will be mailed within 60 days of approval of the 32 mg tablet strength to all EXALGO prescribers and prescribers most experienced in treating chronic pain with extended-release opioid agonists.	
Prescribing Brochure	Education	Prescriber	A, B, C, D, E, F, G, H	The Prescribing Brochure highlights essential information for HCPs who intend to prescribe EXALGO. It is disseminated with all Dear Healthcare Professional Introductory Letters, contained in the Healthcare Professional Education Program Kit, available for distribution by the EXALGO field force, and available for download from www.exalgorems.com .	
Education Confirmation Form (ECF)	Assessment	Prescriber	A, B, C, D, G, H	The Education Confirmation Form (currently the EXALGO Essential Information Form) is intended to confirm education/training in the EXALGO REMS Education Program and is designed to reinforce the most essential information for HCPs who intend to prescribe EXALGO, including risks, safe use, storage and disposal. This form will be modified to include the 32 mg tablet strength and associated risks.	
Safe Use and Handling Guide	Education, Enabler	Patient	A, B, C, D, E, G	The EXALGO Safe Use and Handling Guide is an educational resource to enable prescribers to educate patients on the serious risks and in the safe use, storage, and disposal of EXALGO.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

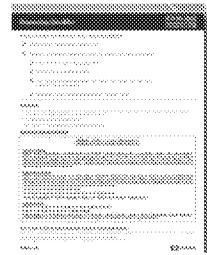
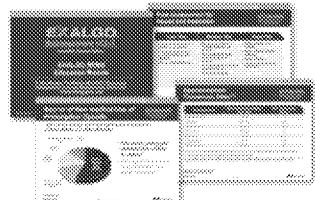
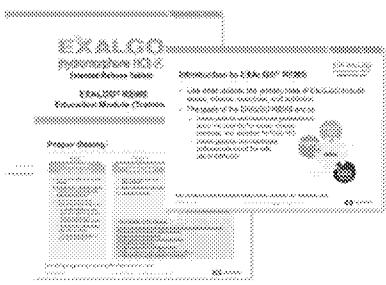
Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

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Tactic	Type	Stakeholder	Content	Brief Description	Image
Education Escalation Program	Education	Prescriber	A, B, C, D, E, F, G, H	The Education Escalation Program uses a structured system to contact identified EXALGO prescribers who have not submitted a completed ECF. Mallinckrodt will continue to evaluate and improve this program to ensure that as many HCPs as possible are educated	
EXALGO REMS Overview Video	Education	Prescriber	A, B, C, D, E, F, G, H	The EXALGO REMS Overview Video is used to introduce the EXALGO REMS program, EXALGO risks, and the EXALGO REMS educational requirements and procedures to potential EXALGO prescribers.	
EXALGO REMS Education Video	Education	Prescriber	A, B, C, D, E, F, G, H	The EXALGO REMS Education Video contains experts in appropriate opioid prescribing (Steven Passik, PhD; Jeffrey Gudin, MD) presenting the EXALGO REMS Education Module and is used to educate potential EXALGO prescribers on EXALGO risks, appropriate prescribing, and safe use..	
Pharmacist Communication Plan	Education	Pharmacist	A, B, C, D, F, G, H	Pharmacists who dispense EXALGO will receive the REMS education material on the risks, appropriate prescribing, and safe use of EXALGO. The Pharmacist Communication Plan will include the Dear Pharmacist Introductory Letter, Prescribing Brochure, EXALGO Safe Use and Handling Guide, EXALGO Dispensing Checklist, and an example of and means to order the Medication Guide Tear Pad.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

Tactic	Type	Stakeholder	Content	Brief Description	Image
Medication Guide Tear Pad	Education	Pharmacist, Patient	A, B, C, D, E, H	The EXALGO Medication Guide will be dispensed with each EXALGO prescription and will provide patients and caregivers with the most important information they should know about EXALGO, including risks, safe use, storage and disposal. Sufficient numbers of Medication Guides will be distributed to all pharmacies that dispense EXALGO. Medication Guide Tear Pads will be available through the product website (www.exalgo.com) and through the Mallinckrodt Call Center.	
EXALGO Dispensing Checklist	Education	Pharmacist	A, C, D, E, G, H	The EXALGO Dispensing Checklist will be used to remind pharmacists of the risks of abuse, misuse, overdose, and addiction of EXALGO. The checklist will also remind pharmacists of the need to dispense a Medication Guide with every prescription, the need to counsel patients and caregivers on safe use, and the requirement that EXALGO is only for opioid-tolerant patients.	
Personal Communications					
EXALGO REMS Education Module	Education	Prescriber, Pharmacist	A, B, C, D, E, F, G, H	The EXALGO REMS Education Module contains all of the information in the Prescribing Brochure and is used to educate potential EXALGO prescribers and allied HCPs on EXALGO risks, appropriate prescribing, and safe use.	
REMS Train-the-Trainer Meeting	Education	Prescriber, Pharmacist	A, B, C, D, E, F, G, H	The Train-the-Trainer Meeting is used to train faculty for the EXALGO REMS education outreach program. The faculty are educated on the EXALGO REMS and all aspects of the EXALGO Full Prescribing Information, clinical trial data, most frequently asked and most important questions regarding appropriate EXALGO prescribing and safe use.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

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Tactic	Type	Stakeholder	Content	Brief Description	Image
EXALGO REMS Education Webinars	Education	Prescriber	A, B, C, D, E, F, G, H	The EXALGO REMS Education Webinars are used to educate potential EXALGO prescribers on EXALGO risks, appropriate prescribing, and safe use. The faculty for this education series are experts in pain medicine and addiction.	
Online Resources					
www.exalgorems.com	Education	Prescriber, Pharmacist, Patient	A, B, C, D, E, F, G, H	The exalgorems.com website contains information about the EXALGO REMS program and serves as one method by which prescribers can complete the EXALGO REMS Education Program. The website serves as a central resource for obtaining all EXALGO REMS educational materials.	
www.exalgo.com	Education	Prescriber, Pharmacist, Patient	A, B, C, D, G, H	The exalgo.com website contains important educational resources for both patients and HCPs, including risk information; proper dosing, administration, and handling of EXALGO; and patient counseling tools for prescribers. The site also contains a dedicated EXALGO REMS section where prescribers can access the EXALGO REMS Educational Program online.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

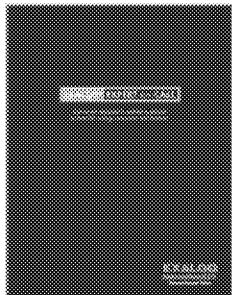
Appendix C: EXALGO-Specific Risk Mitigation Tools and Activities

Tactic	Type	Stakeholder	Content	Brief Description	Image
Print and Video					
EXALGO Dosing and Administration Guide	Education	Prescribers	A, C, D, F, G	The EXALGO Dosing and Administration Guide is a ready-reference tool for prescribers that provides important information about proper patient selection, initiation and titration, safety, and patient counseling information regarding appropriate dosing and administration. The guide will be disseminated to prescribers primarily by the sales force and at congresses.	
Patient Starter Kit and Video	Education	Patient	A, D, G, H	The Patient Starter Kit and Video contains important safety information about the risks and safe use and handling of EXALGO and important risk information, in patient-friendly language. The Patient Starter Kit and Video will be available online and delivered to HCPs via the field force for distribution to patients with their first prescription.	
Personal Communications					
Congress Booth Activities	Education	Prescriber, Pharmacist	A, B, C, D, E, E1, F, G	The EXALGO REMS education material and additional education and outreach material described above will be available at professional congresses for pain specialists. EXALGO REMS faculty will also be available to answer questions. REMS educational material will be available whenever the promotional materials are provided.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

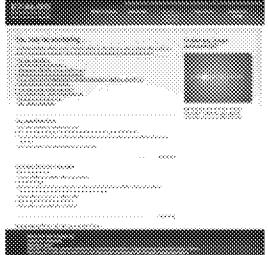
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Tactic	Type	Stakeholder	Content	Brief Description	Image
Expert-on-Call Program	Education	Prescriber, Pharmacist	A, C, D, F	Expert-on-Call is an outreach program that links HCPs who are trained on EXALGO with prescribers who have questions about the product. Prescribers can set up a time for a live call with an “expert” to answer questions and ensure that they understand proper patient selection and dosing for EXALGO, as well as important risk information.	
Mallinckrodt Product Monitoring	Education	Prescriber, Pharmacist, Patient	A, C, D, F	The Mallinckrodt Product Monitoring Department can be reached via a toll-free number (1.800.778.7898) for HCPs and patients to receive more information about EXALGO. This number can also be used to report adverse events or occurrences of abuse or diversion.	
EXALGO Speaker Bureau	Education	Prescriber, Pharmacist	A, C, D, F	EXALGO speakers will be trained on the EXALGO REMS as well as important safety information, dosing, and safe use so that they can give balanced presentations that discuss the benefits as well as the risks associated with EXALGO to an audience of HCPs. Speakers will be trained via live meetings.	
Online Resources					
www.exalgo.com	Education	Prescriber, Patient	A, B, C, D, G, H	The exalgo.com website contains important educational resources for both patients and HCPs, including risk information; proper dosing, administration, and handling of EXALGO; and patient counseling tools for prescribers. The site also contains a dedicated EXALGO REMS section where prescribers can access the EXALGO REMS Educational Program online.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

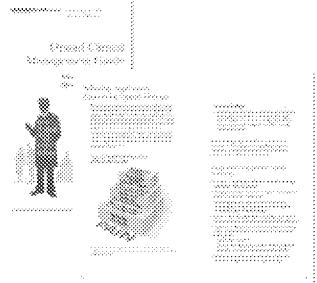
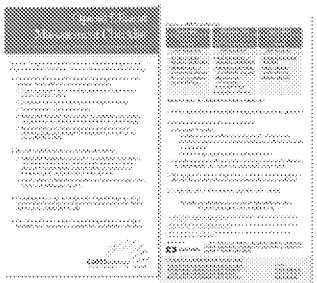
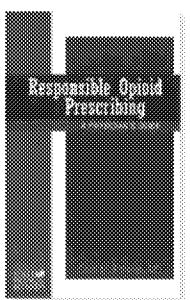
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Tactic	Type	Stakeholder	Content	Brief Description	Image
Answers to Important Questions	Education	Patient	A, C, D, G,	The exalgo.com website contains answers to important questions about EXALGO. These answers describe and reinforce important patient counseling information regarding patient selection and safe use.	
Patient Introductory Video	Education	Patient	A, B, C, D, G, H	The patient video, which presents the most important information on EXALGO risks and safe use, can be accessed through the exalgo.com website.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

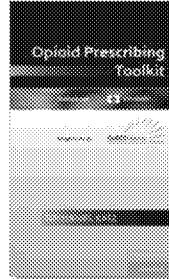
Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

Appendix D: General Opioid Risk Mitigation Tools and Activities

Tactic	Type	Stakeholder	Content	Brief Description	Image
Print and Video					
Opioid Clinical Management Guide	Education	Prescriber, Pharmacist	A, B, C, E, F, G, H	The Opioid Clinical Management Guide is a resource that can help HCPs improve patient outcomes by enhancing knowledge of the potential risks, responsible prescribing, and safe use of opioid pain medications. The guide provides important information on misuse, abuse, addiction, overdose, adverse events, patient selection, patient monitoring, counseling, treatment initiation, and discontinuation.	
Opioid Clinical Management Checklist	Education, Enabler	Prescriber	B, C, E, F, G, H	The Opioid Clinical Management Checklist is a companion to the Opioid Clinical Management Guide. The checklist reinforces documentation, patient selection, risk assessment and stratification, patient counseling, and the 4 A's of patient monitoring (Analgesia, Activities of daily living, Adverse effects, and Aberrant drug-related behaviors) of opioid pain medications.	
<i>Responsible Opioid Prescribing: A Physician's Guide</i>	Education	Prescriber	B, C, E, F, G	<i>Responsible Opioid Prescribing: A Physician's Guide</i> , authored by Scott M. Fishman, MD, provides strategies to aid in the use of prescription opioids for chronic pain and help reduce the risk of addiction, abuse, and diversion when prescribing opioid pain medication. It provides concise steps based on the Federation of State Medical Board's Model Policy for the Use of Controlled Substances for the Treatment of Pain.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

Tactic	Type	Stakeholder	Content	Brief Description	Image
Opioid Prescribing Toolkit	Education	Prescriber	B, C, D, E, F, G	The <i>Opioid Prescribing Toolkit</i> , featuring Nathaniel P. Katz, MD, is a workbook and accompanying CD-ROM that provides a comprehensive array of user-friendly tools to help HCPs safely and effectively prescribe opioid pain medication to patients with chronic pain. Available in print.	
Ask-an-Expert Video: Risk Stratification	Education	Prescriber	B, C, E, F	The Ask-an-Expert video series features experts in the responsible prescribing of opioid analgesics for patients with chronic pain. In the Risk Stratification video, Steven D. Passik, PhD, and Lynn Webster, MD, discuss the importance of thorough assessment of risk for aberrant drug-related behaviors in every patient being considered for opioid therapy. The experts discuss the use of validated risk stratification tools, prescription monitoring programs, and consultation with referring physicians and pharmacies to ensure appropriate use. Available at www.CARESAlliance.org .	
Ask-an-Expert Video: Prescribing Considerations	Education	Prescriber	B, C, D, E, G	The Ask-an-Expert video series features experts in the responsible prescribing of opioid analgesics for patients with chronic pain. In the Prescribing Considerations video, Jeffrey Gudin, MD, discusses the importance of prescribing opioids responsibly, including appropriate patient selection, dosing, and counseling to ensure safe use. Available at www.CARESAlliance.org .	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

Tactic	Type	Stakeholder	Content	Brief Description	Image
APS/AAPM Opioid Treatment Guidelines Reprint Carrier	Education	Prescriber	B, C, E, F, G	The APS/AAPM Opioid Treatment Guidelines Reprint Carrier is an educational tool that provides current, evidence-based recommendations on the use of opioid medications to treat chronic non-cancer pain. Developed by a multidisciplinary expert panel, this resource includes recommendations on all aspects of responsible opioid prescribing: patient evaluation and selection, structuring of opioid therapy to accommodate risk, appropriate initiation and titration, and regular and comprehensive patient monitoring.	
Urine Drug Screening (UDS) Reprint Carrier	Education, Enabler	Prescriber	B, E, F	The UDS Reprint Carrier is an educational tool for prescribers that details the advantages and limitations of UDS and assessment of results using both objective and clinical information. This document contains information on screening for commonly abused drugs, including opioids, alcohol, amphetamines, benzodiazepines, marijuana, and cocaine.	
Universal Precautions in Pain Medicine Reprint Carrier	Education, Enabler	Prescriber	B, C, E, F, G, H	The Universal Precautions in Pain Medicine Reprint Carrier is an educational tool for prescribers consisting of two articles that describe a Universal Precautions approach to the assessment, risk stratification, and ongoing management of patients with chronic pain, including the inherited patient.	

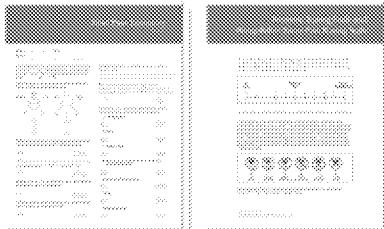
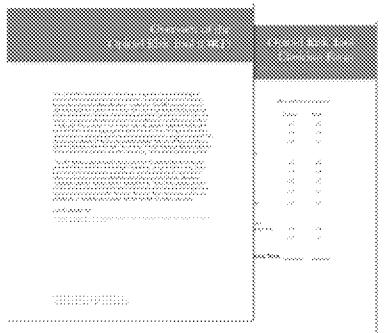
Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

Tactic	Type	Stakeholder	Content	Brief Description	Image
Pain Medicine journal special issue Deaths Related to Opioids Prescribed for Chronic Pain: Causes and Solutions	Education, Enabler	Prescriber	B, E	This collection of journal articles, written by experts in their respective fields and published in a special issue of <i>Pain Medicine</i> (June 2011), represents a starting point for discussion, research, and education about the risks of opioid medications. Available in print.	
Urine Drug Testing (UDT) Brochure	Education, Enabler	Prescriber	B, E	The UDT Brochure is an educational resource for prescribers that reinforces HCP knowledge of when, why, and how to use UDT, including advice about which screen to order. It provides information on the limitations of UDT, how to appropriately interpret results for commonly used drugs, and how to manage the patient-prescriber relationship when ordering UDT.	
Patient-Prescriber Expectations and Responsibilities Form	Education, Enabler	Prescriber, Patient	B, E, F, G, H	The Patient-Prescriber Expectations and Responsibilities Form is a prescriber enabling and patient education resource that helps set expectations for both the patient and the HCP at the start of treatment with an opioid pain medication. This form can provide the foundation for patient counseling opportunities, as well as serve as documentation of patient understanding of risks associated with opioid pain medications, the manner in which the prescription will be obtained from the pharmacy, and the safe use and handling of opioid pain medications.	

Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

Tactic	Type	Stakeholder	Content	Brief Description	Image
Validated Pain Assessment Tools	Assessment, Enabler	Prescriber, Patient	C, F	<p>The Brief Pain Inventory (BPI), Numeric Rating Scale (NRS), and Wong-Baker Faces Pain Rating Scale are validated pain assessment tools for prescribers and patients that have been shown to be effective across a broad range of clinical pain conditions. The NRS and Wong-Baker are unidimensional pain scales. The BPI is a multidimensional tool that assesses pain severity as well as the degree to which pain interferes with functioning. These tools can be used to verify moderate to severe pain during patient selection and track treatment during periodic evaluation.</p> <p>Available at www.CARESAlliance.org.</p>	
Validated Risk Assessment Tools	Assessment, Enabler	Prescriber, Patient	B, C	<p>The Opioid Risk Tool (ORT) and the Revised Screener and Assessment for Patients with Pain (SOAPP®-R) are validated tools for prescribers that can assist in identifying patients who may develop aberrant drug-related behaviors based on known risk factors associated with abuse or addiction. The ORT is a brief 5-question assessment, and the SOAPP-R is a 24-item questionnaire. Both assessments can be self-administered by the patient or completed by the HCP as part of the patient interview.</p> <p>Available at www.CARESAlliance.org.</p>	

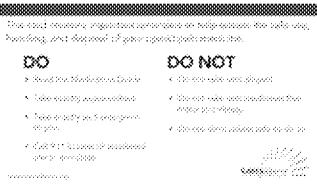
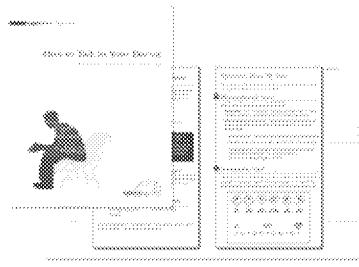
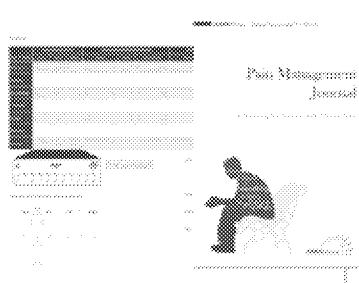
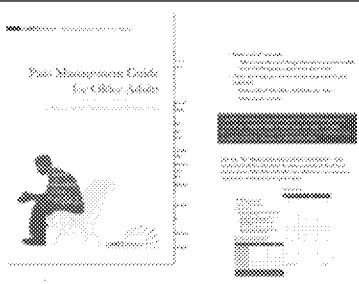
Type: Education, Enabler, Internal Training, Outreach, Independent Medical Education

Educational Content: A=EXALGO Risks, B=Opioid Risks, C=Patient Selection, D=Dosing and Administration, E=General Opioid Use, F=Periodic Evaluation, G=Patient Counseling, H=Providing Medication Guide

Tactic	Type	Stakeholder	Content	Brief Description	Image
Validated Abuse Monitoring Tools	Assessment, Enabler	Prescriber, Patient	B, C, F	The Pain Assessment and Documentation Tool (PADT™) and Current Opioid Misuse Measure (COMM®) are validated tools for prescribers that can assist in identifying aberrant drug-related behaviors associated with abuse or addiction in patients currently receiving chronic opioid therapy. The PADT is a clinician-directed assessment tool that assesses a patient's pain level and the extent to which that pain is being managed by treatment. The COMM is a 40-item questionnaire self-administered by the patient that focuses primarily on current behaviors and cognition.	
Opioid Safe Use and Handling Guide	Education, Enabler	Patient	B, C, D, E, G	The Opioid Safe Use and Handling Guide is an educational resource for patients that describes the serious risks associated with prescription opioid analgesics, such as overdose, misuse, abuse, and addiction, as well as safe use instructions.	
My Meds Card	Education, Enabler	Prescriber, Pharmacist, Patient	B, C, D, E, G	The My Meds Card is included as part of the patient Opioid Safe Use and Handling Guide. It is a wallet-sized card to be used as a patient reference when visiting the HCP or pharmacist. The front side of the card provides space for recording HCP and pharmacy contact information as well as information about any medications (prescription or over-the-counter) the patient is taking. The back side of the card contains patient counseling information on safe use.	

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Tactic	Type	Stakeholder	Content	Brief Description	Image
Safe Use and Handling Card	Education, Enabler	Patient	B, D, E, G	The Safe Use and Handling Card is provided as part of the patient Opioid Safe Use and Handling Guide. Patients who are receiving treatment with opioid analgesics can keep the wallet-sized card for quick reference as an important reminder of safe use conditions necessary to keep themselves, their families, and others safe.	
				Available at www.CARESAlliance.org .	
How to Talk to Your Doctor Brochure	Education, Enabler	Prescriber, Patient	B, C, D, E, G	The How to Talk to Your Doctor Brochure is an educational tool and workbook for patients that describes and identifies information patients should discuss with their doctors in order to optimize clinical outcomes and safe use of prescription opioids.	
				Available at www.CARESAlliance.org .	
Pain Management Journal	Enabler	Prescriber, Patient	E, F, G	The Pain Management Journal is a resource for patients to track their pain and pain management. Filling out the journal can facilitate communication with the HCP, which will optimize the pain management regimen for both the patient and the HCP.	
				Available at www.CARESAlliance.org	
Pain Management Guide for Older Adults	Education, Enabler	Patient	B, C, D, E, G	The Pain Management Guide for Older Adults is a resource for older patients that describes information that can help them to talk openly about their chronic pain with their HCP. This resource also contains information for the patient on how to safely use and handle opioid prescriptions.	
				Available at www.CARESAlliance.org .	

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My Medication Card	Enabler	Prescriber, Pharmacist, Patient	D, E, F	The My Medication Card is included as part of the patient Pain Management Guide for Older Adults. It is intended to be a patient and HCP reference when visiting the HCP or pharmacist. The card provides space for recording HCP and pharmacy contact information as well as information about any medications (prescription or over-the-counter) the patient is taking.	
Available at www.CARESAlliance.org .					
Defeat Chronic Pain Now!	Education	Patient	B, C, D, E, G	Authored by Bradley S. Galer, MD, and Charles E. Argoff, MD, <i>Defeat Chronic Pain Now!</i> provides patients with groundbreaking strategies for eliminating the pain of arthritis, back and neck conditions, migraines, diabetic neuropathy, and chronic illness. The book can also be used by HCPs as a communication resource to their patients. The book specifically discusses commonly misdiagnosed pain conditions and cutting-edge treatments currently under development or on the market.	
Pharmacist's Manual: An Informational Outline of the Controlled Substances Act	Education	Pharmacist	B, C, D, E, F, G	The Pharmacist's Manual is prepared by the Drug Enforcement Agency, Office of Diversion Control, as a guide to assist pharmacists in their understanding of the Federal Controlled Substances Act and in implementing these regulations as they pertain to the pharmacy profession.	
Available at www.CARESAlliance.org .					

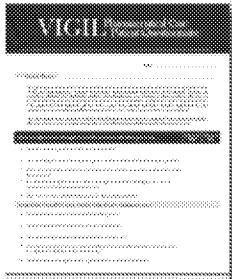
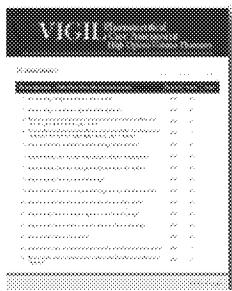
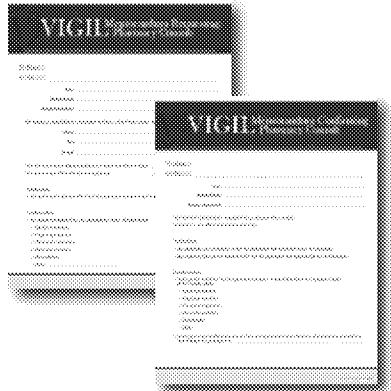
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Tactic	Type	Stakeholder	Content	Brief Description	Image
VIGIL Process Steps	Education, Enabler	Pharmacist	B, C, E, G	The VIGIL Process Steps details some recommended steps that the pharmacist should take when dispensing opioids to patients in order to mitigate the risk of abuse, misuse, and diversion. Steps include Verification, Identification, Generalization, Interpretation, and Legalization (VIGIL). Available at www.CARESAlliance.org .	
VIGIL Documentation Stickers	Enabler	Pharmacist	B, C, E, G	The VIGIL Documentation Sticker is a simple reminder and documentation tool that documents the 5 VIGIL steps for each patient's prescription—Verification, Identification, Generalization, Interpretation, and Legalization. In addition, it allows for an at-a-glance status of a patient's risk level and care level, as well as the need for counseling or Drug Utilization Review. Available at www.CARESAlliance.org .	
VIGIL Designating Agent of Practitioner	Enabler	Pharmacist	E, F	The VIGIL Designating Agent of Practitioner is a form intended for use by HCPs registered with the US Drug Enforcement Agency (DEA) to prescribe opioids under the Controlled Substances Act. With this form, DEA-registered HCPs can authorize another HCP to act as an agent for preparing written prescriptions and communicating these prescriptions to pharmacies. Available at www.CARESAlliance.org .	

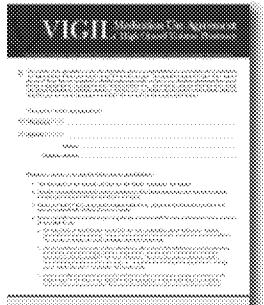
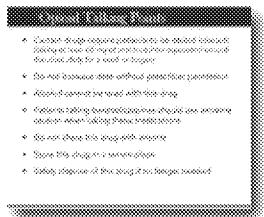
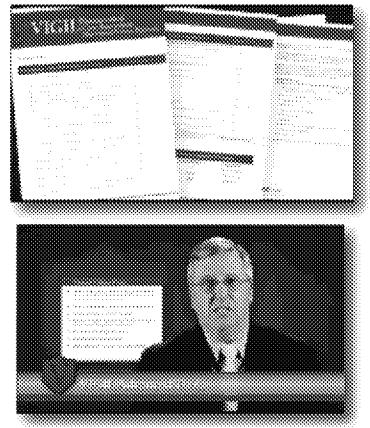
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VIGIL Pharmaceutical Care Patient Questionnaire	Enabler	Pharmacist, Patient	B, C	<p>The VIGIL Pharmaceutical Care Patient Questionnaire is a short questionnaire consisting of 17 items for the patient to answer to help assess his or her risk of abusing opioid pain medications.</p> <p>Available at www.CARESAlliance.org.</p>	
VIGIL Pharmaceutical Care Assessment	Enabler	Pharmacist, Patient	B, C	<p>The VIGIL Pharmaceutical Care Assessment is a questionnaire that can help the pharmacist categorize the level of care required for each patient being prescribed opioid pain medication. It is available in a 12-question short-form for low opioid-volume pharmacies and a longer version for high opioid-volume pharmacies.</p> <p>Available at www.CARESAlliance.org.</p>	
VIGIL Memorandum Requesting/Confirming Pharmacy Consult	Enabler	Prescriber, Pharmacist	C, D, E, F	<p>The VIGIL Memorandum Requesting Pharmacy Consult is a form for use by the pharmacist to request a consultation with the HCP's office regarding a patient's prescription. It can be used to request verification or clarification of prescription details such as opioid-tolerant status, drug name, or potential modifications to the prescription, or to notify the HCP of issues related to the prescription, such as inadequate insurance coverage or legal issues. The VIGIL Memorandum Confirming Pharmacy Consult verifies and documents new or changed prescriptions for opioid medications.</p> <p>Available at www.CARESAlliance.org.</p>	

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VIGIL Medication Use Agreement	Enabler	Pharmacist, Patient	E, G	The Medication Use Agreement is a form used to establish an agreement between the patient and the pharmacist dispensing the prescription. It documents the patient's understanding of his or her responsibilities when taking the medication and the pharmacist's responsibilities when dispensing it. Available at www.CARESAlliance.org .	
VIGIL Opioid Talking Points	Education, Enabler	Pharmacist, Patient	B, D, E, G	The VIGIL Opioid Talking Points is a 4" x 3.5" sticker that lists the most important safety facts that pharmacists should share with patients before dispensing opioid pain medication. Bulleted points are written in simplified language to help ensure that the patient understands how to take opioid pain medication safely. Available at www.CARESAlliance.org .	
VIGIL Education and Implementation Video	Education	Pharmacist	B, C, E, F, G	In this brief video, David Brushwood, RPh, JD, discusses the conflicting therapeutic imperatives faced by pharmacists dispensing opioids to patients with chronic pain in a highly regulated environment. The ethics of pain management; potential "red flags" for misuse, abuse, or diversion of pain medications; and adherence to Drug Enforcement Administration regulations on dispensing controlled substances are also described. A program is introduced that can improve compliance with responsible opioid dispensing practices—Verification, Identification, Generalization, Interpretation, and Legalization (VIGIL) and provides background on the VIGIL process and the available VIGIL tools. Available at www.CARESAlliance.org .	

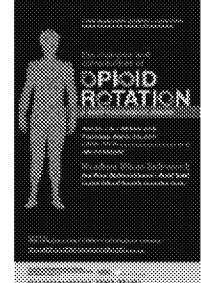
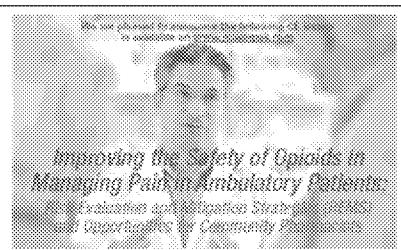
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Personal Communications					
CARES Alliance Education Train-the-Trainer Meeting	Education, Outreach	Prescriber	A, B, C, E, F, G, H	Expert faculty in the fields of pain and addiction medicine were trained in order to facilitate education of HCPs on responsible opioid prescribing and use. All faculty participating in congress booth activities were trained in August 2010.	
Congress Booth Activities	Education, Outreach	Prescriber, Pharmacist	A, B, C, D, E, F, G, H	The EXALGO REMS education material and additional education and outreach material described above will be available at professional congresses for pain specialists. EXALGO REMS faculty will also be available to answer questions. REMS educational material will be available whenever the promotional materials are provided.	
Overcoming Barriers to the Balanced Management of Chronic Pain—Path of the Patient: Managing Chronic Pain in Primary Care	Independent Medical Education	Prescriber	B, C, D, E, F, G	This 60-minute interactive Web-based activity is being co-supported with Purdue Pharma and will be made available to HCPs on PriMed.org and ChronicPainTX.org. The activity will launch in September 2011.	
EPIC (Empowering Peers to Improve Care) Pain Management Mentoring Network	Independent Medical Education	Prescriber	E	The EPIC Pain Management Mentoring Network is designed to help provide HCPs with the necessary education and resources needed to improve pain management. The program includes a performance improvement initiative; small-group peer workshops led by renowned experts; and a resource center offering video blogs, current publications, sample tools, and links to current standards of care resources and practice guidelines. A total of 100 participants have enrolled to date, and the program will launch in September 2011.	

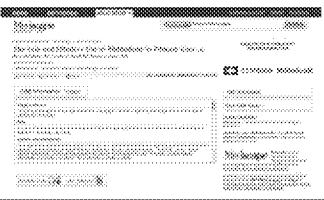
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PEERSpectives in Chronic Pain	Independent Medical Education	Prescriber	E	PEERSpectives in Chronic Pain is an interactive panel discussion based on content presented at the 2011 American Pain Society annual scientific conference and is being co-supported by Endo Pharmaceuticals and NeurogenX. The activity launched on July 29, 2011 on www.cmezone.com with 134 HCPs completing the activity as of September 12, 2011, with 12 certificates issued.	
The Nuances and Complexities of Opioid Rotation: A Point-Counterpoint Debate	Independent Medical Education	Prescriber	C, D, E, F	The Point-Counterpoint Debate took place as a satellite symposium at the American Academy of Pain Management meeting on March 24, 2011. A total of 185 HCPs attended, and the enduring piece launched on July 20, 2011. As of September 12, 2011, a total of 48 HCPs have completed the program, and 14 certificates have been issued.	
National Association of School Nurses—Unintended Consequences: Prescription Drug Abuse in Our Schools and Communities	Independent Medical Education	Prescriber	B, C, D, E, F, G	The Unintended Consequences symposium took place in July 2011 and was attended by more than 900 school nurses. This project, co-supported with Pfizer, Cephalon, and Endo Pharmaceuticals, will be expanded into an online monograph to be released in the fall of 2011.	
Improving the Safety of Opioids in Managing Pain in Ambulatory Patients: Risk Evaluation and Mitigation Strategies (REMS) and Opportunities for Community Pharmacists	Independent Medical Education	Pharmacist	B, C, D, E, F, G, H	This program is a Web-based clinical dialog launched on August 11, 2011 on www.powerpak.com providing information on implementing and maximizing REMS within the pharmacy setting. To date, 722 HCPs have completed the activity, with 522 certificates issued.	

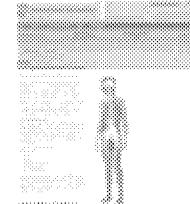
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Pain and Pain Management: How to Manage Opioid Risk	Independent Medical Education	Prescriber	B, C, D, E, F, G, H	This program is a live, non-certified medical education satellite symposium being held at the 18th Napa Pain Conference in September 2011. A total of 300 participants are expected to attend.	
The Safe and Effective Use of Methadone in Primary Care	Independent Medical Education	Prescriber	B, C, D, E, F, G, H	This program is a Web-based continuing medical education spotlight being hosted on www.medscape.com. It was released in September 2010. As of September 2011, a total of 11,492 participants have completed the program, and 3331 certificates have been issued.	
Clinicians' Forum—Pain Management and Risk Mitigation: A Practical Approach	Independent Medical Education	Prescriber	B, C, D, E, F, G, H	This educational program is a live symposium held in conjunction with the American Pain Society annual scientific meeting in May 2011. A total of 98 clinicians attended the program, which was co-supported by Purdue Pharma.	
Online Resources					
www.CARESAlliance.org	Education, Enabler	Prescriber, Pharmacist, Patient	B, C, D, E, F, G, H	To enhance the responsible prescribing and safe use of opioid pain medications, C.A.R.E.S. Alliance seeks members and support from multiple groups, including healthcare professionals, people with pain, pharmacists, professional societies, pharmaceutical companies, and other organizations focused on patient safety. C.A.R.E.S. Alliance is based on the belief that the answer to effective pain management lies in education, innovation and collaboration between health care professionals and people with pain. To this end, www.CARESAlliance.org provides a central location for access to the prescriber, patient, and pharmacist tools described in this table.	

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American Chronic Pain Association Patient Resources	Education, Enabler, Assessment	Patient		www.CARESAlliance.com provides links to online patient resources from the American Chronic Pain Association. Patient resources include an online pain log, quality of life scales, and important reminder and follow-up guides to help patients remember and follow instructions from doctors and pharmacists.	

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